content. TGF-β1 gene expression is almost 3-fold increased in patients with multiple vs single restenosis events in sapheneous vein grafts. Overall, extracellular neo-matrix formation was continuously increased over time.

4:30

803-3 Influence of Presence or Absence of Medial Necrosis on Endothelial Regeneration and Intimal Hyperplasia in the Rabbit Carotid Artery

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Interventional injury induced intimal hyperplasia (IH) involves smooth muscle cell proliferation which may be limited by endothelial cell (EC) regeneration. We hypothesized that EC-regeneration (ECR) modulates IH. To create different ECR's we induced EC removal with 100% media necrosis (2F Fogarty balloon, 5 cm) and without media necrosis (prolene loop, 5 cm) in the rabbit carotid artery. After termination at 3, 7, 21 or 42 days, the artery was divided in segments which were alternately processed for paraffin- and frozen sections. ECR was assessed with an antibody to CD31 and expressed as percentage coverage. Proliferating cells were identified with an antibody to the nuclear antigen Ki-67 and scored as percentage positive cells. The cross-sectional IH area (IHA, mm^2) was measured morphometrically from elastin stained sections. *Results:* Wall coverage (%) with CD31 positive cells, IHA (mm^2) (mean ± sem, * = $p < 0.05$, † = $p < 0.001$, Fogarty balloon (BAL) versus loop):

	n	ECR,3d	ECR,7d	ECR,21d	ECR,42d	IHA,7d	IHA,21d	IHA,42d
BAL	7	3 ± 2	57 ± 14	61 ± 5	82 ± 11	0.01 ± 0.01	0.20 ± 0.01*	0.26 ± 0.03†
loop	7	8 ± 4	81 ± 10	93 ± 4	100 ± 0	0.01 ± 0.01	0.09 ± 0.04	0.08 ± 0.02

From 3–42 days, ECR was enhanced in loop versus balloon injured arteries ($P < 0.001$, ANOVA). At 3 and 7 days, more medial proliferation was found after balloon than after loop injury (3d: 46.2 ± 8.8% versus 0.2 ± 0.1%, 7d: 18.5 ± 6.4% versus 1.0 ± 0.4%; $p < 0.01$, ANOVA). In the same period, abundant adventitial proliferation was found after balloon injury which was entirely absent after loop injury.

Conclusion: Endothelial cell regeneration is slower over a damaged than over a normal media. This retarded endothelial cell regeneration may contribute to enhanced intimal hyperplasia.

4:45

803-4 Very Early Noninvasive Visualization of Experimental Atherosclerosis with Chimeric Antibody Z2D3 Radiolabeled with In-111 via Negatively-Charged Chelating Polymer, or Tc-99m via Glucarate Transchelation

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We had reported the feasibility of noninvasive imaging of experimental atherosclerotic lesions with Indium-111-labeled mouse/human chimeric Z2D3 $F(ab')_2$ specific for proliferating smooth muscle cells in human atheroma. Lesions were visualized by 48 H. To reduce the delay between visualization and antibody administration, (i), Z2D3 $F(ab')_2$ was labeled with In-111 via negatively-charged chelating polymers (specific activity 500–1300 MBq/mg) and compared to the conventional In-111 labeled counterpart (specific activity 32–48 MBq/mg); and (ii), Z2D3 Fab' was labeled with Tc-99m via a weak transchelator, glucaric acid.

In vivo targeting was evaluated in 16 rabbits with atherosclerotic lesions induced by infradiaphragmatic balloon deendothelialization of the abdominal aorta followed by hyperlipidemic diet for 12 weeks. Four rabbits received 24 MBq (50 μg) of In-111-charge modified Z2D3 $F(ab')_2$. Two rabbits received 130 MBq (100 μg) of the kit formulation of this preparation. Six rabbits received 24 MBq (500–750 μg) of conventional Z2D3 $F(ab')_2$. The remaining 4 animals received Tc-99m Z2D3 Fab' (500–600 Mbq/375 μg). Gamma imaging revealed unequivocal tracer uptake in the abdominal atherosclerotic lesions at 24 H in all 4 animals injected with modified Z2D3. In 2 rabbits with higher specific radioactivity, the *lesions could be visualized at 3 H*. The blood pool activity in rabbits injected with the conventional Z2D3 did not permit definitive visualization of the lesions before 48 H. Blood clearance was significantly faster with modified Z2D3 (0.10 ± 0.008, Mean %ID/g ± SEM), as compared to the conventional Z2D3 (0.29 ± 0.04; $p < 0.01$). Uptake of modified Z2D3 preparations in atherosclerotic lesions at 24 H (0.08 ± 0.01) was similar to the conventional Z2D3 at 48 H (0.08 ± 0.02; p = NS). Tc-Fab' localization was visualizable at 12 H after administration of antibody. The Tc-Fab' uptake in the atherosclerotic lesion was significantly higher in the lesion (0.022 ± 0.004) compared to the normal (0.013 ± 0.002; $p = 0.04$) aorta. This study demonstrated the feasibility of very early noninvasive visualization of atherosclerotic lesions with antibody-based scintigraphy.

804 Treatment in Unstable Angina

Wednesday, March 22, 1995, 4:00 p.m.–5:00 p.m.
Ernest N. Morial Convention Center, La Louisiane B

4:00

804-1 Heparin Pretreatment May Confer Additional Benefit in Patients Treated with 7E3 and PTCA for Unstable Coronary Syndromes

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Patients undergoing percutaneous intervention for unstable coronary syndromes associated with coronary thrombus are at substantially increased risk of ischemic complications. The incidence of ischemic complications in the EPIC trial was reduced in this subgroup (n = 893) by treatment with the chimeric monoclonal anti-IIb/IIIa antibody 7E3. We assessed the clinical effects of heparin pretreatment in this group. Data were available for 855 patients of whom 583 received 7E3 bolus or bolus and infusion. Of these, 383 (66%) were pretreated with heparin for a mean 55 hours [interquartile range 21, 96]. Outcomes examined included the primary 30 day composite endpoint (death, non-fatal infarction, CABG, repeat percutaneous intervention for acute ischemia) components thereof and major bleeding events.

	Pretreatment		
	Heparin (n = 383)	No heparin (n = 200)	Odds ratio (95% CI)
Primary endpoint	30 (7.8%)	25 (12.5%)	1.7 (0.9, 2.9)
Repeat percutaneous intervention or CABG	11 (2.9%)	10 (5.0%)	1.8 (0.7, 4.3)
Myocardial infarction	14 (3.7%)	13 (6.5%)	1.8 (0.8, 4.0)
Major bleeding event	20 (5.2%)	14 (7.0%)	1.3 (0.7, 2.8)

There was a strong trend toward further reduction of ischemic endpoints when patients received heparin pretreatment in addition to 7E3. This effect was not associated with an increased incidence of significant bleeding. These data support further investigation of the potentially additive roles of anti-platelet and anti-thrombotic treatments as adjuncts to percutaneous intervention in unstable coronary syndromes.

4:15

804-2 Low Molecular Weight Heparin, Regular Heparin or Aspirin to Treat Silent Ischemia in Unstable Angina

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We report a randomized prospective single blind study to test if low molecular weight heparin (LMWH) in a high dose (214 IC/kg anti-Xa, b.i.d.) by subcutaneous injection may achieve a potential benefit over regular heparin (RH) and or aspirin to reduce silent events and its complications. A total of 205 patients with angina at rest in the last 24 hrs before admission entered the study. Patients were monitored using a 2 channel device provided with an alarm signal system during the first 48 hrs and randomized to aspirin in a dose of 200 mg (Group A), aspirin plus RH (400 IU/kg/day i.v. trited by aPTT [Group B]) and aspirin plus LMWH (Group C). The end points were: (1) free of silent and symptomatic events; (2) recurrent angina, (3) AMI, (4) urgent intervention ([UI] PTCA or CABG), (5) major bleeding and (6) death. A total of 8234 hrs were recorded appropriately. Events rates were tested by two-tailed chi-square:

Groups		No Events		Recurrent Angina		AMI		UI	
G	n	n	p	n	p	n	p	n	p
A	69	28 (40%)	0.0002*	13 (19%)	0.1	4 (6%)	0.3	1 (1%)	0.6
B	69	27 (39%)	0.00001†	18 (26%)	0.01‡	1 (1%)		3 (4%)	
C	67	49 (73%)		6 (9%)		0		0	

*C vs A, †C vs B, ‡C vs B

Minor bleeding was detected in 10 cases in group B and 1 in C ($p = 0.006$). There was only 1 major bleeding in group B and no deaths in any group. *Conclusions:* In this study, treatment with LMWH in a high dose plus aspirin reached significantly better results than aspirin alone or aspirin plus RH.